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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/059,521	01/29/2002	Ivan N. Rich	R103 1030.1	5794

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EXAMINER	
GABEL, GAILENE	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 02/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/059,521	RICH, IVAN N.	
	Examiner	Art Unit	
	Gailene R. Gabel	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28,31,42-44,57 and 58* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-28,31,42-44,57 and 58* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on December 5, 2005 has been entered.

Amendment Entry

2. Applicant's amendment and arguments, filed on December 5, 2005, is acknowledged and has been entered. Claims 29, 30, 32-41, and 45-56 have been cancelled. Claims 1, 42, and 44 have been amended. Claims 57 and 58 have been added. Accordingly, claims 1-28, 31, 42-44, 57, and 58 are pending and are under examination.

Withdrawn Rejections

3. All rejections not reiterated herein, have been withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-28, 31, 42-44, 57, and 58 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites the limitation "cell growth medium comprising fetal bovine serum having a concentration of between 0% and 30% and methyl cellulose having a concentration of between about 0.4% and about 0.7%, and transferrin and in an atmosphere having between about 3.5% oxygen and 7.5% oxygen" in step a). There is insufficient antecedent basis for this particular combination of specific elements in a cell growth medium in the specification.

New Matter

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-28, 31, 42-44, 57, and 58 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

In this case, the specification does not appear to provide literal or adequate descriptive support for the recitation of "cell growth medium comprising fetal bovine serum having a concentration of between 0% and 30% and methyl cellulose having a concentration of between about 0.4% and about 0.7%, and transferrin and in an atmosphere having between about 3.5% oxygen and 7.5% oxygen" in step a). Nowhere in Applicant's disclosure appears to provide or teach such particular combination of the specific elements in a cell growth medium. None of the originally filed claims also recited the limitation in question. The particular combination of elements in the culture growth medium as recited in claim 1, does not flow from the specification and is therefore considered to encompass new matter. See In re ANDERSON, 176 USPQ 331 (CCPA 1973). Recitation of claim limitations lacking literal or adequate descriptive support in the specification or originally filed claims constitutes new matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 1-28, 31, 42-44, 57, and 58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Crouch et al. (Journal of Immunological Methods, 160: 81-88 (1993)) in view of Bell et al. (US 2002/0120098 A1) and in further view of Moore et al. (US Patent 5,328,844).

Crouch et al. disclose an assay method for determining the proliferative status, i.e. cell proliferation, of a population of primitive hematopoietic cells. The hematopoietic cells are granulocyte-macrophage colony-forming cells (GM-CFC) and granulocyte colony-forming cells (G-CFC), i.e. TF-1 and NFS-60 cells, isolated from human peripheral blood, and are detected for cytokine dependent proliferation by stimulation of granulocyte-macrophage colony stimulating factor (GM-CSF) and granulocyte colony stimulating factor (G-CSF) (see Abstract). Initially, the hematopoietic cell lines from peripheral blood are cultured and maintained in a cell growth culture medium containing 0% to 30% (12.5%) fetal bovine serum (fetal calf serum). Crouch et al. then isolate mononuclear cells (MNCs) from peripheral blood, i.e. containing hemoglobin, in order to render the MNC sample substantially free of hemoglobin. Crouch et al. isolate the MNCs by Ficoll-Hypaque density gradient centrifugation. For ATP bioluminescence assay, Crouch et al. specifically contacts the isolated MNCs with luciferin-luciferase monitoring reagent which generates bioluminescence in the presence of adenosine triphosphate or ATP (see page 81, column 2 and page 82, columns 1 and 2). The amount of luminescence generated by the reagent indicates the amount of ATP in the MNC cell population, wherein the amount of ATP indicates the proliferative status of the hematopoietic cells.

Crouch et al. differ from the instant invention in failing to disclose that the cell growth culture medium includes methyl cellulose having a concentration of about 0.4% to 0.7%, transferrin, and maintained in an atmosphere having between about 3.5% to 7.5% oxygen. Crouch et al. also does not teach generating a hematopoietic population

enriched in progenitor cells and stem cells from animal tissue such as bone marrow, fetal liver, and spleen, isolated from cow, sheep, pig, horse, goat, dog, cat, and primates, and determining their suitability for transplantation, and isolating and identifying specific subpopulations of primitive hematopoietic cells using cell surface markers. Lastly, Crouch et al. does not teach contacting the hematopoietic cells with a test compound and determining its ability to modulate proliferation of the cells.

Bell et al. disclose compositions and methods comprising heme-containing components for use in inducing and/or enhancing stimulation of hematopoiesis (erythropoiesis), in order to hence, stimulate erythroid progenitor proliferation in a cell culture system. Hematopoiesis involves the proliferation of hematopoietic stem cells and hematopoietic progenitor cells and the stimulation is specific for hematopoietic colony-forming cell erythroid macrophage, megakaryocyte stem cells (CFC-GEMM) (see page 4, column 1, [0026], page 7, column 2, [0071], and page 9, column 2, [0085]). According to Bell et al., the burst forming unit-erythroid (BFU-E) represents the most primitive hematopoietic or erythroid progenitor and forms large multi-clustered hemoglobinized colonies (see page 1, column 1, [0004]). In practice, Bell et al. teach culturing the primitive hematopoietic cells in a cell growth medium comprising 30% fetal bovine serum, about 0.4% to about 0.7% (0.8%) methyl cellulose which increases viscosity in culture media, and in an atmosphere having between about 3.5% to 7.5% (5%) oxygen. Bell et al. also teach contacting the sample with cytokine such as GM-CSF and Flt3 Ligand to generate a cell population substantially enriched in CFC-GEMM stem cells for use in cell proliferation assay (see page 7, column 2, [0071], page 9,

column 2, [0084-0092], and Examples 1 and 2). According to Bell et al., erythroid progenitor colony formation is enhanced at lower, more physiological oxygen tensions, such as 5% oxygen (see page 11, column 1, [0098-0101]. These enriched hematopoietic stem cells or progenitor cells are obtained from bone marrow, cord blood, or peripheral blood, and if determined to have adequate proliferative status, can be transplanted into a recipient patient (see page 4, column 2, [0030] and page 7, column 2, [0078]). Hematopoietic stem cells or progenitor cells can also be obtained and enriched from animal tissue such as bone marrow, cord blood, fetal liver, or spleen, of dog, cow, horse, cat, pig, sheep, goat, chicken, primate, or human (see page 8, column 2, [0076-0078]). Subpopulations of primitive hematopoietic cells are characterized by the presence of specific hematopoietic progenitor cell surface markers such as CD34 and glycophorin A (see page 12, column 1, [0105]). These cell subpopulations can be selectively isolated and purified from other cells (cord blood) and other [heme-containing] sample components by binding the cells with antibodies specific for their cell surface markers such as anti-CD34 and anti-glycophorin A or by magnetic bead separation, i.e. STEMSEP^{TM} system, and other separation systems, i.e. CEPRATE LC system, and selectively determining their identity by flow cytometry or flow activated cell sorting (see page 17, column 1, [0144 and 0145] and Example 9). Bell et al. further teach contacting primitive hematopoietic cells having a target cell population with a test a compound (Ganciclovir) and determining its ability to modulate, i.e. inhibit, proliferation or differentiation of the target cell population. Result of the testing is compared with negative control (see Example 11).

Moore et al. disclose the beneficial effect of iron-saturated transferrin in mammalian cell growth media. Moore et al. specifically taught that when iron-saturated transferrin is added, other iron salts are not required. According to Moore et al., the function of transferrin in culture growth media is to act as an iron transport protein for the cells. See column 13, lines 52-65 and column 14, lines 30-44.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to substitute the culture growth media composition as taught by Bell having 30% fetal bovine serum, 0.8% methyl cellulose, and in an atmosphere having between about 5% oxygen, and to include therein transferrin taught by Moore, for the culture system as taught by Crouch for maintaining cells suitable for ATP bioluminescence assay, because Bell specifically taught that hematopoietic progenitor cells or stem cells favor survival and growth in a medium having such composition for use in any proliferation assays. One of ordinary skill in the art at the time of the instant invention would have been motivated to incorporate the culture system as taught by Bell and complimented with transferrin by Moore, which stimulates proliferation of hematopoietic cells culture growth media, for subsequent use as MNC sample for testing proliferation status using the ATP bioluminescence assay as taught by Crouch, because methyl cellulose is conventionally known to advantageously increase viscosity of proliferating cells in culture media, and transferrin as taught by Moore is conventionally known to advantageously provide iron protein transport for cells in the media, and Bell specifically taught that erythroid progenitor colony formation is even further enhanced at lower, more physiological oxygen tensions, i.e. 5% oxygen; hence,

increasing the concentration of hematopoietic progenitor cells for use in assays that measure proliferation of cell populations, including the ATP bioluminescence assay taught by Crouch.

Response to Arguments

7. Applicant's arguments with respect to claims 1-28, 31, 42-44, 57, and 58 have been considered but are moot in view of the new ground(s) of rejection.

8. No claims are allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (571) 272-0820. The examiner can normally be reached on Monday, Tuesday, and Thursday, 7:00 AM to 4:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gailene R. Gabel
Patent Examiner
Art Unit 1641
February 18, 2006